Estimating Cancer Mortality Rates from SEER Incidence and Survival Data

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Synopsis

A method to estimate site-specific cancer mortality rates using Surveillance, Epidemiology, and End Results (SEER) Program incidence and survival data is proposed, calculated, and validated. This measure, the life table-derived mortality rate (LTM), is the sum of the product of the probability of being alive at the beginning of an interval times the probability of dying of the cancer of interest during the interval times the annual age-adjusted incidence rate for each year that data have been collected. When the LTM is compared to death certificate mortality rates (DCM) for organ sites with no known misclassification problems, the LTM was within 10 percent of the death certificate rates for 13 of 14 organ sites. In the sites that have problems with the death certificate rates, there were major disagreements between the LTM and DCM. The LTM was systematically lower than the DCM for sites if there was overreporting on the death certificates, and the LTM was higher than the DCM for sites if there was underreporting. The limitations and applications of the LTM are detailed.

STATISTICS ON CANCER incidence, survival, and mortality are reported annually by the National Cancer Institute (NCI) (*1*). The cancer incidence and survival data are collected by the Surveillance, Epidemiology, and End Results Program (SEER) of NCI. Since 1973, these data have been reported to NCI by central cancer registries in selected geographic areas containing about 10 percent of the United States population. In contrast, the cancer mortality rates are calculated from the underlying cause of death listed on death certificates. Mortality data are collected for the total United States by the National Center for Health Statistics (NCHS).

A number of authors have pointed out the inaccuracies of death certificates listing cancer as the underlying cause of death (*2-4*) by comparing these to the diagnoses determined by autopsy of the deceased. In a recent study by NCI, the accuracy of mortality data has been studied by comparing the cause of death on death certificates to hospital records of diagnoses (*5*). In this study the underlying cause of death as coded on the death certificate was found to be accurate for about 65 percent of the deaths attributed to cancer when detailed sites are used. Disagreements in classification appeared most often for certain sites, such as overreporting of cancers of the colon and liver and underreporting of cancer of the rectum and oral (buccal) cavity.

Clearly, another way of estimating mortality rates is desirable. Several studies have proposed using life table methods on incidence and survival data to estimate the number of deaths caused by cancer (*6,7*). We propose, calculate, and validate a life table-derived mortality rate (LTM) derived solely from population-based or SEER-determined incidence and survival data.

Materials and Methods

The cancer incidence and survival rates are based on data from the SEER Program of the NCI. The data used in this analysis were from 1973-83 SEER information on cases of cancer diagnosed among residents of Hawaii, Connecticut, Iowa, New Mexico, Utah, Atlanta, Detroit, Seattle-Puget Sound, and San Francisco-Oakland. The cancer site-specific rates are for all races with both sexes combined unless the site was sex-specific; for these sites the sex-specific rates were used. The rates are for malignant tumors only and exclude in-situ lesions.

Survival rates. Site-specific, cumulative observed survival rates and interval relative survival rates for first primary tumors by year since diagnosis from 1973 to 1983 are used in the analysis (*8*). These rates exclude second or later primary tumors and death certificate only cases for the period 1973–83.

The cumulative observed survival rate from diagnosis to $k-1$ years after diagnosis for calendar year j, $CP_{k,j}$, is the probability of surviving all causes of death from the date of diagnosis to the beginning of interval k for a site-specific cancer case.

The interval relative survival rate for interval k is the probability of escaping death from cancer during the interval k. This probability is estimated by the interval relative rate ($R_{k,j}$) which is obtained by dividing the observed survival rate of the cohort of interest by the survival rate for 1 year of a sample of the U.S. population matched to the patient cohort by age, race, sex, and calendar year. Hence, the relative survival rate is a ratio of observed to expected survival rates (*9*).

Mortality rates. The death certificate-derived mortality rates (DCM) are age-adjusted to the 1970 United States population by the direct method using vital statistics collected by the NCHS. SEER-area mortality rates (SEER DCM) are also from NCHS data but have been selected for the SEER geographic areas only.

Cancer incidence. Annual cancer incidence rates for first primary tumors that are site-specific and age-adjusted are used in the analysis. The rates for 1973–83 are age-adjusted using the direct method for the 1970 United States population and are similar to those published for the years 1973–81 (*10*). Second and later primaries and death certificate only cases are not counted as incident cancers. The same criteria are also used for the survival rates so that they would be consistent with the incidence rates.

The life table-derived mortality rate. The life table-derived age-adjusted mortality rate (LTM) for calendar year j is given as

$$M_j = \sum_{k=0}^{j-1} I_{j-k}\, CP_{k,j-k}\, [1 - R_{k,j-k}] \qquad [1]$$

where

M_j = Age-adjusted mortality rate per 100,000 for calendar year j.

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I_{j-k} = Age-adjusted annual incidence rate for calendar year $j-k$.

$CP_{k,j-k}$ = Cumulative observed survival rate for calendar year of diagnosis $j-k$.

$R_{k,j-k}$ = Probability of surviving the site-specific cancer during the interval k for calendar year $j-k$, given one is alive at the beginning of the interval. This measure is called the interval relative survival rate.

j = 1 for calendar year 1973, 2 for 1974 . . . 11 for 1983.

The LTM is a function of the sum of the product of the annual age-adjusted incidence rate (I_{j-k}) times the probability of being alive at the beginning of a period ($CP_{k,j-k}$) times the probability of dying of the site-specific cancer during the period ($1-R_{k,j-k}$) for each year data have been collected. Since the last two terms represent the formulation of life table calculations, the LTM can be viewed as a function of life table-weighted annual incidences. A sample calculation for LTM is given in the Statistical Notes, page 38.

Since the LTM relies on a cumulative measure of the incidence and survival data for estimating mortality, the LTM requires a number of years of data to give an accurate estimate. Table 1 reports the number of years required for the LTM to be within 10 percent of the DCM for those sites with no known misclassification problems. On average, 6 years were required for the LTM to converge to within 10 percent of the DCM.

The age-adjusted incidence rates are a summary measure of a spectrum of age-specific rates. As a consequence, there may be a problem in that this summary measure is too crude a measure of the effects of age-specific incidences. To examine em-

Calculation of LTM Using Age-specific Incidence and Survival Rates

Let the number of deaths of the cancer of interest (D'_{jl}) for age group, l, for calendar year j be:

$$D'_{jl} = \sum_{k=0}^{j-1} N_{j-k,l}\, CP_{k,j-k,l}\, [1 - R_{k,j-k,l}]$$

Then for the case of using age-specific rates and aging the cases, the number of deaths of the cancer of interest (D''_{jl}) for age group, l, for calendar year j is:

$$D''_{jl} = \sum_{k=0}^{j-1} \left\{ (1 - F_{j-k,l})\, N_{j-k,l}\, CP_{k,j-k,l}\, [1 - R_{k,j-k,l}] + (F_{j-k,l-1})\, N_{j-k,l-1}\, CP_{k,j-k,l-1}\, [1 - R_{k,j-k,l-1}] \right\}$$

where

$N_{j-k,l}$ = Number of incident cases in age group, l;, with the cancer of interest in calendar year $j-k$.

$CP_{k,j-k,l}$ = Cumulative observed survival rate for age group, l, beginning at time period k for the calendar year of diagnosis $j-k$.

$R_{k,j-k,l}$ = Probability of surviving the site-specific cancer for age group, l, during the interval k for calendar year $j-k$. This measure is called the age-specific interval relative survival rate.

$F_{j-k,l}$ = Fraction of age group l that move to an older age group.

Age-adjusted mortality rates (standardized to 1970 US population) are determined as:

$$M_j = \sum_{l=1}^{11} (D_{jl}\, P_{jl}) \div U_l$$

where

P_{jl} = Age-specific population at risk (in this case the population of the SEER areas used in the study) for calendar year j.

U_l = proportion of 1970 US population in each age group per million.

pirically the appropriateness of using the age-adjusted incidence rates, a more detailed analysis was performed to determine the effect of using age-specific rates and aging the cases (that is, allow the cases to contribute in several age-specific categories). Two analytical approaches were taken.

The first involved the use of calendar-year and age-specific survival rates on the number of newly diagnosed cases in an age group. The number of deaths in an age group was determined using the method reported in the Statistical Notes (page 38), which is similar to the method for computing equation 1. Age-specific data for the observed and relative interval survival were used, and the number of cases in an age group was substituted for the age-adjusted rates to determine the number of deaths in an age group. The age-specific mortality was determined from the number of deaths in an age group and the SEER area population data by age and calendar year. These age-specific rates were converted to age-adjusted rates using the 1970 U.S. population as the standard.

In the second method, the number of incident cases were aged after diagnosis so that a portion of the cases in one age group were moved into an older age group before dying. For example, of the 1973 incident cases in the age range of 35–39, .217 were 39 years old. Thus, after the second year, .217 of the mortality due to cases diagnosed in this age group was moved to the 40–44 age group. Similarly a portion of the 40–44 age group contributed to the 45–49 age group. Then these deaths were converted to age-specific rates by calendar year, using SEER population data, and they were standardized to the 1970 U.S. population to create age-adjusted rates (see Statistical Notes, page 39). Breast cancer was chosen as the site for this detailed analysis because its long survival allows the potential for significant contributions due to aging.

Results

Site-specific SEER incidence rates (SEER INCID), United States mortality rates (US DCM), SEER-area mortality rates (SEER DCM), and life table mortality rates (LTM) are shown in figure 1.

In order to measure the accuracy of the LTM, a comparison of the 1983 LTM and SEER-Area

Sample Calculation for Breast Cancer LTM

I. SEER breast cancer incidence for first primary cancers

Year of diagnosis	1973	1974	1975	1976	1977	1978	1979	1980
Incidence rate:	75.77	85.90	79.33	77.49	75.34	74.87	75.82	75.64

II. Cumulative observed survival rates (SEER)

Years since diagnosis	*Year of diagnosis*							
	1973	*1974*	*1975*	*1976*	*1977*	*1978*	*1979*	*1980*
0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1	.916	.920	.927	.927	.925	.927	.929	.931
2	.832	.841	.852	.852	.855	.852	.849	.857
3	.758	.773	.782	.782	.783	.777	.773	.782
4	.700	.706	.724	.716	.716	.715	.708	.716
5	.641	.652	.673	.663	.664	.656	.651	.656
6	.591	.608	.625	.614	.617	.609	.600	
7	.549	.567	.585	.572	.576	.565		
8	.516	.532	.550	.534	.536			
9	.484	.502	.516	.493				
10	.456	.471	.478					

III. $1 - R$ values (1 – interval relative survival rates) (SEER)

Years since diagnosis	*Year of diagnosis*							
	1973	*1974*	*1975*	*1976*	*1977*	*1978*	*1979*	*1980*
1	.0641	.0598	.0517	.0533	.0538	.0521	.0496	.0475
2	.0710	.0649	.0611	.0611	.0549	.0602	.0646	.0478
3	.0680	.0610	.0620	.0609	.0633	.0653	.0667	.0660
4	.0569	.0668	.0515	.0640	.0628	.0576	.0616	.0601
5	.0620	.0539	.0466	.0522	.0490	.0570	.0553	.0606
6	.0554	.0453	.0468	.0492	.0462	.0469	.0526	
7	.0490	.0432	.0389	.0444	.0405	.0462		
8	.0357	.0359	.0322	.0407	.0424			
9	.0352	.0292	.0337	.0513				
10	.0315	.0348	.0446					

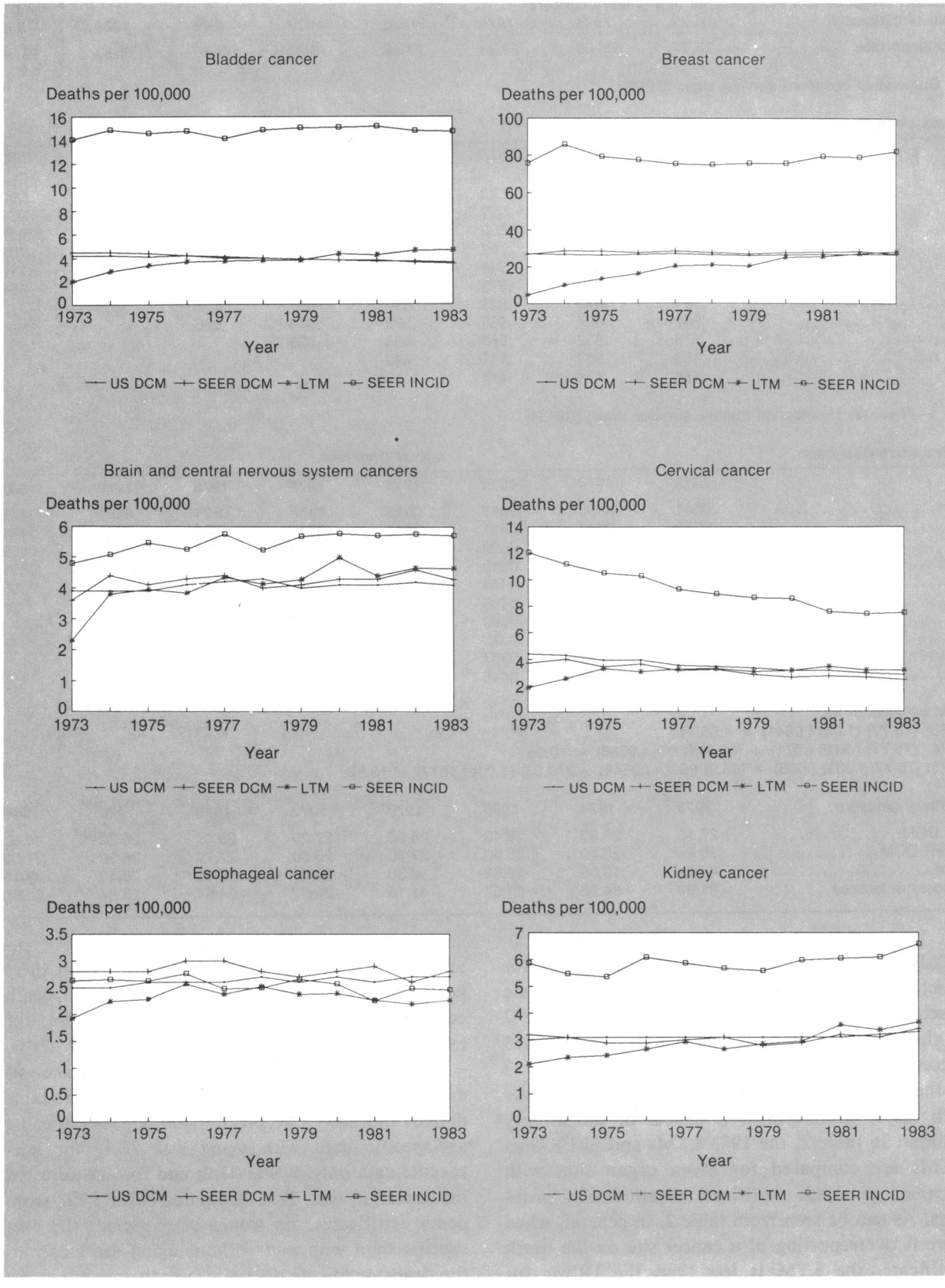
LTM calculation for:
1973: (75.77) (1.00) (.0641) = 4.86
1974: (75.77) (.916) (.071) + (85.9) (1.00) (.0598) = 10.06
1975: (75.77) (.832) (.068) + (85.9) (.920) (.0649) + (79.33) (1.00) (.0517) = 13.52

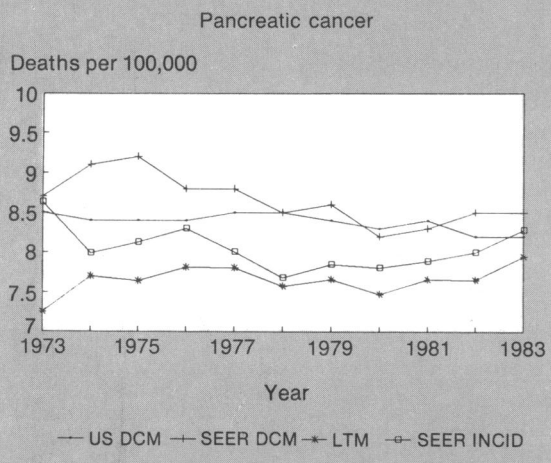
Mortality Measure	*1973*	*1974*	*1975*	*1976*	*1977*	*1978*	*1979*	*1980*
US DCM	27.10	26.80	26.40	26.80	27.20	26.60	26.20	26.60
SEER DCM	26.90	28.70	28.50	27.70	28.50	27.70	26.90	27.60
LTM	4.86	10.06	13.52	16.30	20.36	20.90	20.49	25.15
Percent difference	−81.94	−64.93	−52.57	−41.16	−28.57	−24.54	−23.84	−8.88

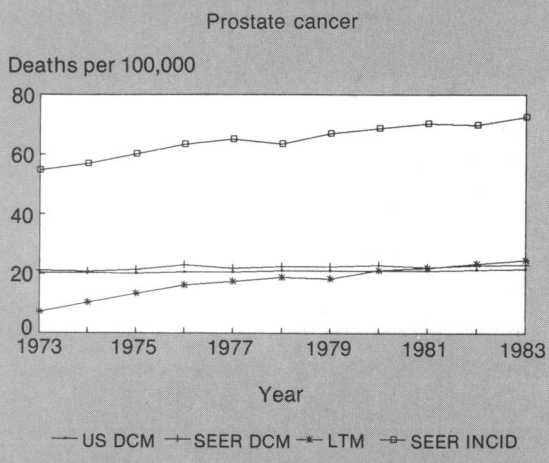
DCMs is given in table 1 for 14 organ sites for which there are no known major death certificate misclassification problems (*5*). In summary, for 2 of the 14 sites examined, the LTMs are within 5 percent of the SEER-area mortality rates, and 13 of the 14 sites are within 10 percent. The lone site with major disagreement is cancer of the urinary bladder. In table 2, the 1983 LTMs and SEER-area DCMs are compared for seven organ sites with documented death certificate classification problems. As can be seen from table 2, in general, when there is overreporting of a cancer site on the death certificate, the LTM is less than the DCM; for example, colon, liver, and esophagus. When there is underreporting of the organ site on the death certificate, the LTM is greater than the DCM; for example, cervix, oral cavity, rectum, and testis.

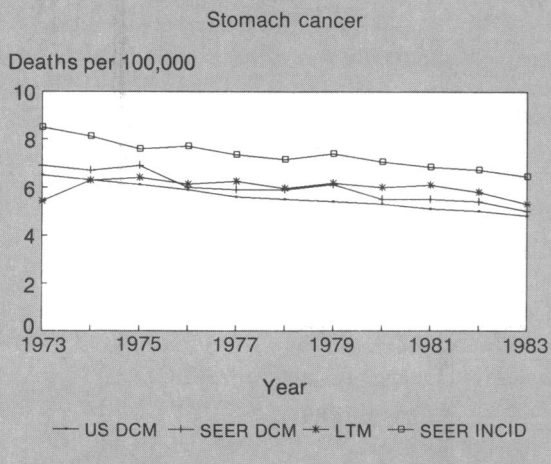
The results of the age-specific incidence analysis are shown in figure 2. For 1983, the life-table derived mortality rate per 100,000 population using age-specific data with aging was 26.2; for age-specific data only, it was 27.2; and for age-adjusted incidence, it was 28.4 compared with 27.0 from death certificates. As would be expected, the age-specific data with and without aging are closer to the death certificate data.

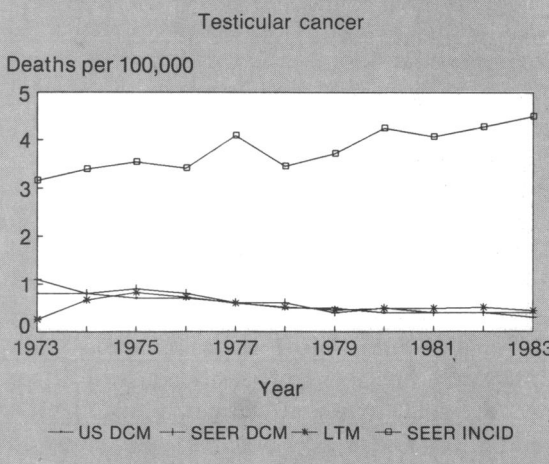
Figure 1. Cancer incidence and mortality rates for 18 sites

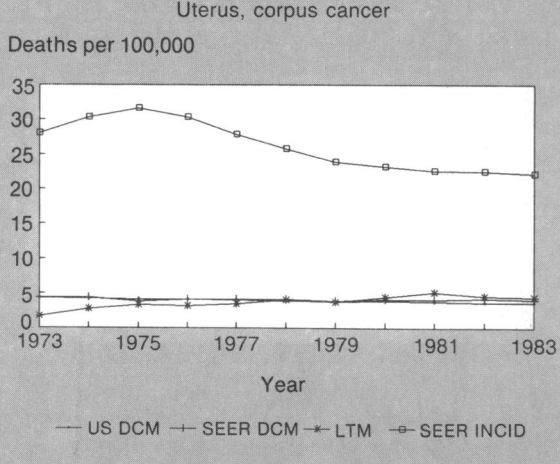


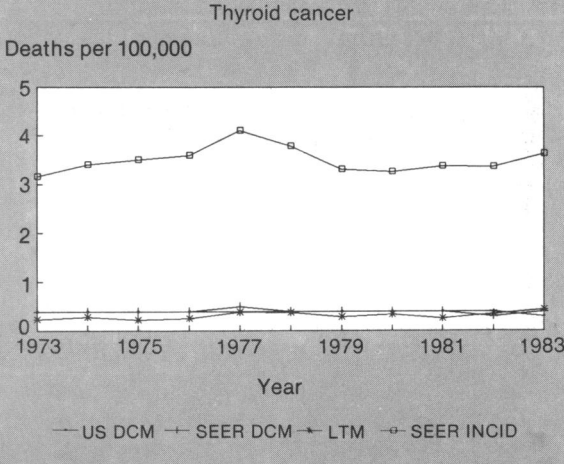

Pancreatic cancer
Deaths per 100,000
10
9.5
9
8.5
8
7.5
7
1973
1975
1977
1979
1981
1983
Year
US DCM
SEER DCM
LTM
SEER INCID


Prostate cancer
Deaths per 100,000
80
60
40
20
0
1973
1975
1977
1979
1981
1983
Year
US DCM
SEER DCM
LTM
SEER INCID

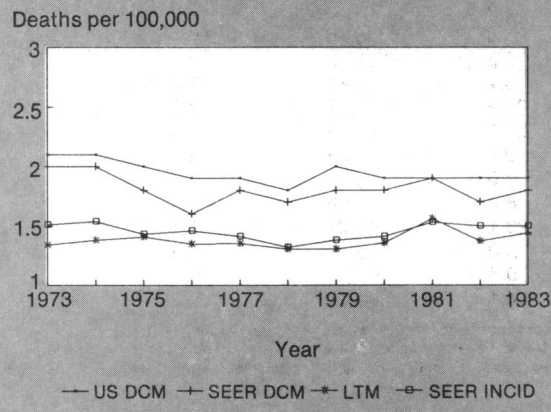

Stomach cancer
Deaths per 100,000
10
8
6
4
2
0
1973
1975
1977
1979
1981
1983
Year
US DCM
SEER DCM
LTM
SEER INCID


Testicular cancer
Deaths per 100,000
5
4
3
2
1
0
1973
1975
1977
1979
1981
1983
Year
US DCM
SEER DCM
LTM
SEER INCID

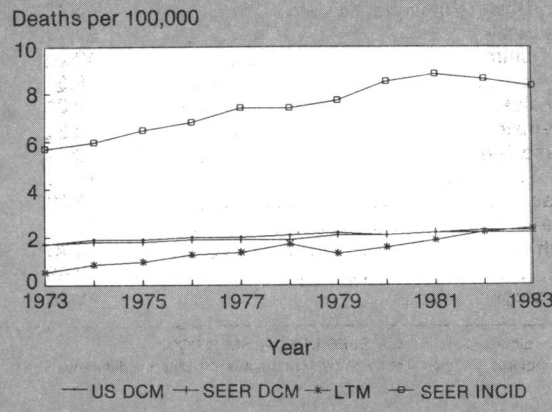

Uterus, corpus cancer
Deaths per 100,000
35
30
25
20
15
10
5
0
1973
1975
1977
1979
1981
1983
Year
US DCM
SEER DCM
LTM
SEER INCID


Thyroid cancer
Deaths per 100,000
5
4
3
2
1
0
1973
1975
1977
1979
1981
1983
Year
US DCM
SEER DCM
LTM
SEER INCID

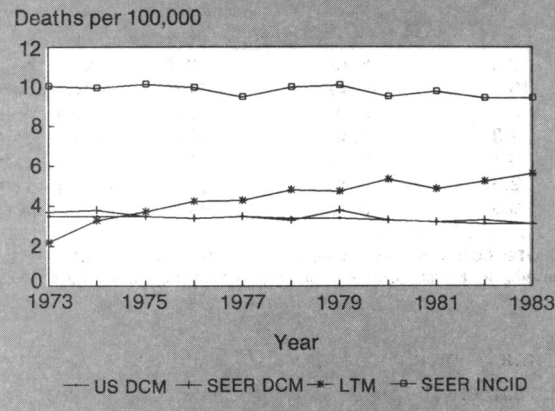
Liver cancer



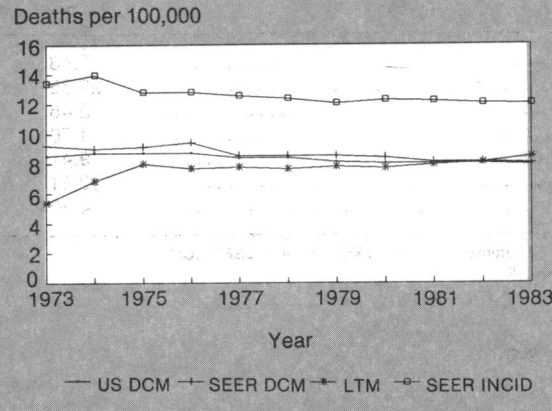
Melanoma of the skin



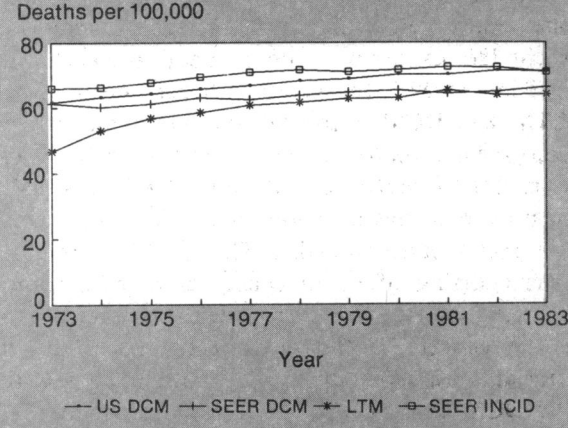
Oral cavity cancer



Ovarian cancer



Lung cancer in white males



Lung cancer in white females

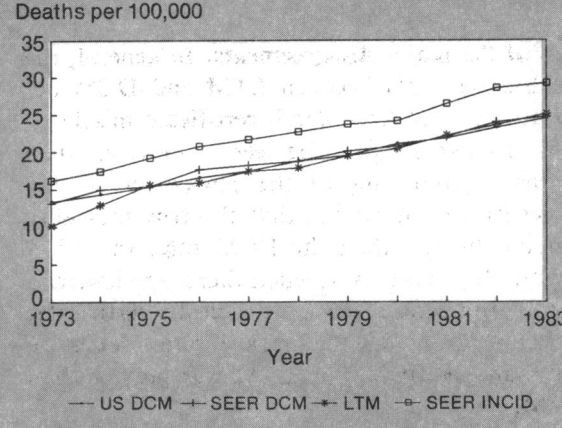


Table 1. Comparison of mortality rates for 1983 for organ sites with no misclassification problems

Organ	Incidence	SEER DCM	SEER LTM	Percent difference[1]	Years for 10 percent difference[2]
Bladder	14.73	3.5	4.65	32.8	NA
Brain and central nervous system	5.72	4.3	4.65	8.2	3
Breast (female)	82.30	27.0	28.38	5.1	8
Colon, rectum	42.26	19.8	21.40	8.1	5
Kidney	6.58	3.4	3.65	7.4	4
Lung (males)	70.85	66.2	64.00	-3.3	3
Lung (females)	29.20	24.7	25.07	1.5	3
Melanoma (skin)	8.34	2.2	2.38	8.2	10
Ovary	11.98	8.0	8.43	5.4	5
Pancreas	8.28	8.5	7.95	-6.5	8
Prostate	72.45	23.1	24.73	7.1	8
Stomach	6.45	5.0	5.30	5.9	2
Thyroid	3.63	0.4	0.44	9.7	11
Uterus, corpus	22.16	4.1	4.41	7.5	6

[1] Percent difference = (LTM - SEER DCM) ÷ SEER DCM.
[2] Years required for the LTM to show less than a 10 percent difference with DCM.

NOTE: DCM = death certificate mortality; LTM = life table mortality; SEER = Surveillance, Epidemiology, and End Results Program, National Cancer Institute.

Table 2. Comparison of mortality rates for 1983 for sites with misclassification problems

Organ	Incidence	SEER DCM	SEER LTM	Percent difference[1]	Death certificate misclassification[2]
Cervix	7.48	2.4	3.13	30.3	Underreported
Colon	29.75	16.9	14.44	-14.6	Overreported
Esophagus	2.45	2.8	2.26	-19.4	Overreported
Liver	1.50	1.8	1.44	-20.0	Overreported
Oral cavity	9.41	3.1	5.63	81.5	Underreported
Rectum	12.51	2.9	6.95	139.8	Underreported
Testis	4.50	0.3	0.44	45.2	Underreported

[1] Percent difference = (LTM - SEER DCM) ÷ SEER DCM.
[2] Reference 5.

NOTE: DCM = death certificate mortality; LTM = life table mortality; SEER = Surveillance, Epidemiology, and End Results Program, National Cancer Institute.

Discussion

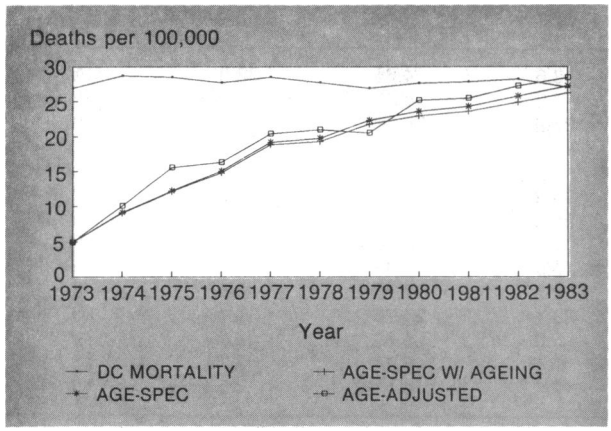
The sources of differences between LTMs and DCMs will be discussed first, then the limitations of LTM are enumerated, and finally potential uses of LTM will be outlined.

Sources of the major disagreements. In general, the major disagreements between LTM and DCM occurred at sites that have death certificate misclassification problems. As can be seen in table 2, when there was overreporting of the cancer site on the death certificate, indicating that the true mortality rate should be less than the DCM rate, the LTM was below the DCM. And when there was underreporting of the cancer site on the death certificate, indicating that the true mortality rate should be greater than the DCM, the LTM was greater than the DCM.

Two sites, esophagus and liver, have death certificate mortality rates that are greater than their first primary incidence rates. These results indicate a fundamental problem with the death certificate mortality since one would expect their cancer mortality rate to be less than their incidence rates. For liver cancer, this occurs, in part, because liver cancer is listed as the underlying cause of death on the death certificate even though it may be a secondary cancer or a site of metastasis (*11*).

The site with the greatest disagreement between LTM and DCM is the rectum. Percy and coworkers (*5*) have reported that rectal cancer is underreported as a cause of death and is misclassified on death certificates as colon cancer for 30 percent of the rectal cancer deaths. This problem results in overreporting of colon cancer and underreporting of rectal cancer. As a consequence of overreporting colon cancer on the death certificates, the true mortality rate for this cancer should be less than the DCM rate. The LTM is lower than the DCM rate. The underreporting of rectal cancer causes the true cancer mortality rate to be greater than the

Figure 2. Comparison of four rates of breast cancer mortality from SEER areas



DC mortality is SEER area death certificate mortality, AGE-SPEC. is the mortality rate calculated using age-specific incidence and survival rates, AGE-SPEC W/ AGEING is the mortality calculated using the age-specific rates and ageing the cases, and AGE-ADJUSTED is the LTM.

Table 3. Death certificate data for 1978–82

Site	Total cases	Death certificate only	
		Number of cases	Percent of total
Bladder	18,031	76	0.42
Brain and central nervous system	6,141	92	1.50
Breast (female)	51,049	371	0.73
Cervix	5,875	37	0.63
Colon	39,317	369	0.94
Colon, rectum	55,693	433	0.77
Esophagus	3,977	47	1.18
Kidney	7,422	56	0.75
Liver	2,395	82	3.42
Lung (males)	39,701	480	1.21
Lung (females)	17,312	211	1.22
Oral cavity	12,663	52	0.41
Ovary	7,866	53	0.67
Pancreas	10,280	195	1.90
Prostate	35,895	250	0.70
Rectum	16,376	64	0.39
Stomach	9,980	141	1.41
Testis	2,263	3	0.13
Thyroid	4,483	9	0.20
Uterus, corpus	14,593	70	0.48

SOURCE: Reference *15*.

DCM for this site. The LTM is higher than the DCM for rectal cancers.

The combination of the two sites removes the misclassification problem for death certificates (*5*). The LTM rates for the combined sites are within 10 percent of the DCM rates after 5 years, confirming the previous report by Percy (*5*). The colon, rectal, and colorectal cancer incidence and mortality rates that illustrate these points are plotted in figure 3. Percy postulates that physicians have changed their methods of recording the diagnoses when they fill out the death certificates. The discrepancies between death certificates and hospital records for the oral cavity and testis could have simlar etiologies.

For the cervix, for which there is underreporting on death certificates, the underlying cause of death on the death certificate is not specific enough to identify the definitive site. Uterine cancers, or uterus, NOS, on a death certificate can mean either cancer of the cervix uteri or corpus uteri (*12*). In the late 1970s, more than 25 percent of the uterine cancer deaths reported on death certificates were not specified as either cervix uteri or corpus uteri.

Limitations of the LTM. The calculation of LTM requires three components: population-based annual incidence rates, the cumulative observed survival rates of the cancer cases, and their interval relative survival rates. Each component has its own idiosyncrasies and can contribute to erroneous estimates of mortality.

The annual incidence rates used to calculate the LTM are based on first primary cancers only. A source of disagreement occurs if a cancer patient has a second or later primary cancer that is more likely to be the underlying cause of death on the death certificate. In this case, the LTM underestimates the true cancer mortality rate. For example, women with colorectal cancer are at an increased risk of developing independent primary cancers of the breast, uterine corpus, and ovary (*13–14*).

A further source of error that might occur because of the use of first primary incidence rates is the fact that death certificate-derived mortality rates represent death certificate-only cases while LTM excludes these cases. This problem is site specific, averaging about 1 percent of the total cases. Table 3 gives the percentage of death certificate-only cases by anatomic site (*15*). Liver has the greatest fraction of death certificate-only cases—3.42 percent.

The observed survival rates can also be a source of error. The observed rates are derived from those people who are diagnosed with cancer at a SEER registry and followed until death. The fraction of patients lost to followup will affect the estimates of the observed rates. A source of discrepancy between the LTM and DCM occurs when SEER area patients migrate outside the SEER area and die. The patients will be followed by SEER and will be included as contributing to the LTM. However, the death certificate mortality data will exclude these subjects from the SEER area data since the patients

have migrated out of the area. In addition, cancer patients that migrate into a SEER area will not be counted in the LTM but will be included in the DCM rates for the SEER area. Insomuch as there is an imbalance between in-migration and out-migration in the SEER area, discrepancies in the two rates can be envisioned. The true mortality for the SEER area is all those who died of the cancer while resident in the area. As a consequence, the LTM overestimates the true mortality rate if there is an excess of cancer patients outmigrating and underestimates the true rate if there is an excess of inmigrating cancer patients. This phenomenon is a particular problem for sites with long survival times such as breast, thyroid, and cervical cancer.

Finally, the interval-relative survival rates can also be a source of error. A problem may occur when the general population adjustment is inappropriate. Using the expected rates from the total U.S. population assumes that the patient group is a random sample from the total population. If patients with cancer die from noncancer causes that are different from those of the U.S. population, the interval-relative survival may be a source of error. For example, persons with lung cancer are generally smokers with multiple health problems, and their noncancer mortality rates are higher than those of the U.S. population. As a consequence, the U.S. population adjustment overestimates their survival. When this happens, the interval relative survival rates are a source of error.

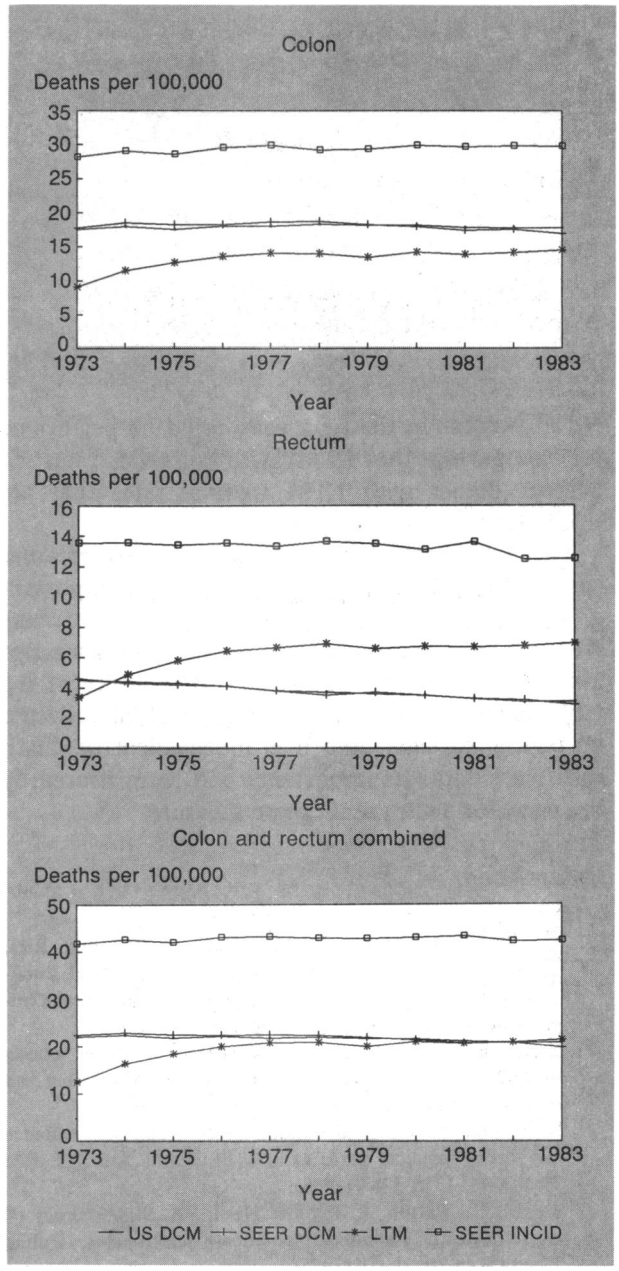
Given these potential limitations, the LTM has a number of potential uses.

Potential uses of LTM. The development of a mortality measure using only SEER incidence and survival is important for a number of reasons. First, when there are known misclassification problems with death certificates at specific sites, such as oral cavity, colon, rectum, and others, the LTM may be used as a more accurate measure of their mortality rates than the DCM. This can be done because the SEER incidence and survival data are independent of the death certificate data, and therefore they allow a complementary measure of mortality.

Second, the LTM allows predicted estimates of mortality by extent of disease (stage), histologic type, or treatment because the SEER data include hospital data, which may not be available from death certificates. Of course, validation studies will be needed to determine the accuracy of these predicted estimates.

Third, divergence between the LTM and DCM could be used as a management tool to identify

Figure 3. Cancer incidence and mortality rates for the colon, rectum, and colon and rectum combined



potential problems. This divergence could alert managers of possible problems that could be caused by either the LTM or DCM. A candidate for possible further examination is cancer of the bladder. The major disagreement in LTM and DCM for this site portends possible classification problems.

Fourth, the LTM can be used to measure the impact of early detection or treatment. For example, an estimate of the impact of increasing survival

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by 20 percent in the next year could be performed by comparing the LTM with survival rates 20 percent higher with LTM survival rates that are unchanged.

The LTM offers an alternate way to measure cancer mortality. Such an alternative is important if there are problems with the death certificate measure or if mortality data by subgroups are not available from death certificates. The utility of the LTM is that it uses data and information collected on cancer patients, and it is independent of death certificate data. Its importance will be measured by the need for such an alternate measure.

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